10/681,637R>

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
NEWS	4	OCT 28	KOREAPAT now available on STN
NEWS	5	NOV 30	PHAR reloaded with additional data
NEWS	6	DEC 01	LISA now available on STN
NEWS	7	DEC 09	12 databases to be removed from STN on December 31, 2004
NEWS	8	DEC 15	MEDLINE update schedule for December 2004
NEWS	9	DEC 17	ELCOM reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	10	DEC 17	COMPUAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	11	DEC 17	SOLIDSTATE reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	12	DEC 17	CERAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	13	DEC 17	THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB
NEWS	14	DEC 30	EPFULL: New patent full text database to be available on STN
NEWS	15	DEC 30	CAPLUS - PATENT COVERAGE EXPANDED
NEWS	16	JAN 03	No connect-hour charges in EPFULL during January and February 2005
NEWS	17	FEB 25	CA/CAPLUS - Russian Agency for Patents and Trademarks (ROSPATENT) added to list of core patent offices covered
NEWS	18	FEB 10	STN Patent Forums to be held in March 2005
NEWS	19	FEB 16	STN User Update to be held in conjunction with the 229th ACS National Meeting on March 13, 2005
NEWS	20	FEB 28	PATDPAFULL - New display fields provide for legal status data from INPADOC
NEWS	21	FEB 28	BABS - Current-awareness alerts (SDIs) available
NEWS	22	FEB 28	MEDLINE/LMEDLINE reloaded
NEWS	23	MAR 02	GBFULL: New full-text patent database on STN
NEWS	24	MAR 03	REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS	25	MAR 03	MEDLINE file segment of TOXCENTER reloaded

NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN

10/681,637R>

NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 19:25:30 ON 10 MAR 2005

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 19:25:39 ON 10 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 9 MAR 2005 HIGHEST RN 844817-50-1
DICTIONARY FILE UPDATES: 9 MAR 2005 HIGHEST RN 844817-50-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\10681637.str

chain nodes :
10 11 12 15 16 20 21

10/681,637R>

ring nodes :
1 2 3 4 5 6 7 8
chain bonds :
3-12 4-11 5-15 5-16 7-20 7-21 8-10
ring bonds :
1-2 1-5 2-3 3-4 3-6 4-5 4-8 6-7 7-8
exact/norm bonds :
1-2 1-5 2-3 3-4 3-6 3-12 4-5 4-8 4-11 5-15 5-16 6-7 7-8 7-20 7-21
8-10

G1:OH,NH

G2:O,S,N

G3:H,O,OH,Cy,Ak

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 10:CLASS 11:CLASS
12:CLASS 15:CLASS 16:CLASS 20:CLASS 21:CLASS

L1 STRUCTURE UPLOADED

=> s l1
SAMPLE SEARCH INITIATED 19:26:06 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1972 TO ITERATE

50.7% PROCESSED 1000 ITERATIONS 1 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

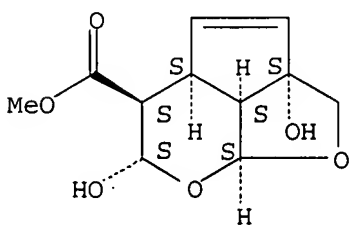
FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 36777 TO 42103
PROJECTED ANSWERS: 1 TO 123

L2 1 SEA SSS SAM L1

=> d scan

L2 1 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
IN 2H-1,7-Dioxacyclopent[cd]indene-5-carboxylic acid, 2a,4a,5,6,7a,7b-hexahydro-2a,6-dihydroxy-, methyl ester, (2aS,4aS,5S,6S,7aS,7bS)- (9CI)
MF C11 H14 O6

Absolute stereochemistry.



10/681,637R>

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

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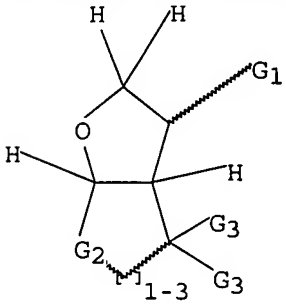
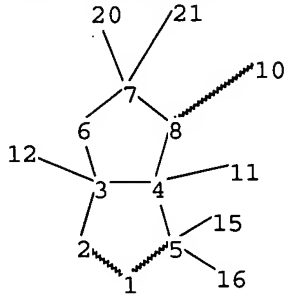
Uploading C:\Program Files\Stnexp\Queries\106816371.str





chain nodes :
10 11 12 15 16 20 21
ring nodes :
1 2 3 4 5 6 7 8
chain bonds :
3-12 4-11 5-15 5-16 7-20 7-21 8-10
ring bonds :
1-2 1-5 2-3 3-4 3-6 4-5 4-8 6-7 7-8
exact/norm bonds :
1-2 1-5 2-3 3-4 3-6 3-12 4-5 4-8 4-11 5-15 5-16 6-7 7-8 7-20 7-21
8-10
isolated ring systems :
containing 1 :

G1:OH,NH

G2:O,S,N

G3:H,O,OH,Cy,Ak

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 10:CLASS 11:CLASS
12:CLASS 15:CLASS 16:CLASS 20:CLASS 21:CLASS

L3 STRUCTURE UPLOADED

=> s l3
SAMPLE SEARCH INITIATED 19:28:04 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1972 TO ITERATE

50.7% PROCESSED 1000 ITERATIONS 1 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

10/681,637R>

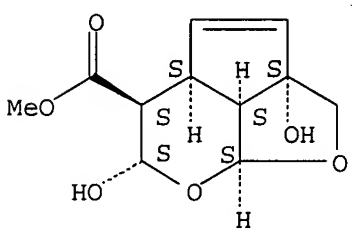
FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 36777 TO 42103
PROJECTED ANSWERS: 1 TO 123

L4 1 SEA SSS SAM L3

=> d scan

L4 1 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
IN 2H-1,7-Dioxacyclopent[cd]indene-5-carboxylic acid, 2a,4a,5,6,7a,7b-hexahydro-2a,6-dihydroxy-, methyl ester, (2aS,4aS,5S,6S,7aS,7bS)- (9CI)
MF C11 H14 O6

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=> s l3 ful
FULL SEARCH INITIATED 19:28:27 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 39427 TO ITERATE

100.0% PROCESSED 39427 ITERATIONS 75 ANSWERS
SEARCH TIME: 00.00.02

L5 75 SEA SSS FUL L3

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	163.05	163.26

FILE 'CAPLUS' ENTERED AT 19:28:36 ON 10 MAR 2005

10/681,637R>

26, 1996), unless otherwise indicated in the original publications.
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FILE COVERS 1907 - 10 Mar 2005 VOL 142 ISS 11
FILE LAST UPDATED: 9 Mar 2005 (20050309/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

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=> s l5
L6          76 L5

=> s l6 and (process or prepara? or synthes? or make or made)
       2058963 PROCESS
       1372174 PROCESSES
       3061803 PROCESS
                 (PROCESS OR PROCESSES)
       1436714 PREPARA?
       2556211 PREPN
        198603 PREPNS
       2706663 PREPN
                 (PREPN OR PREPNS)
       3469141 PREPARA?
                 (PREPARA? OR PREPN)
       1432482 SYNTHES?
        205351 MAKE
        158511 MAKES
        353636 MAKE
                 (MAKE OR MAKES)
       1137894 MADE
            23 MADES
       1137914 MADE
                 (MADE OR MADES)
L7          51 L6 AND (PROCESS OR PREPARA? OR SYNTHES? OR MAKE OR MADE)

=> s l7 and (photochemical or irradiat?)
         43562 PHOTOCHEMICAL
            15 PHOTOCHEMICALS
         43577 PHOTOCHEMICAL
                 (PHOTOCHEMICAL OR PHOTOCHEMICALS)
        146742 PHOTOCHEM
            55 PHOTOCHEMS
        146764 PHOTOCHEM
                 (PHOTOCHEM OR PHOTOCHEMS)
        158881 PHOTOCHEMICAL
                 (PHOTOCHEMICAL OR PHOTOCHEM)
        281810 IRRADIAT?
        295396 IRRADN
          3221 IRRADNS
        296450 IRRADN
                 (IRRADN OR IRRADNS)
        451350 IRRADIAT?
                 (IRRADIAT? OR IRRADN)
L8           5 L7 AND (PHOTOCHEMICAL OR IRRADIAT?)
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10/681,637R>

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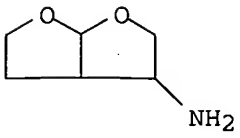
=> s l7 and 1,3-dioxolane
       8199662 1
       6242831 3
         14395 DIOXOLANE
          2142 DIOXOLANES
         14898 DIOXOLANE
                 (DIOXOLANE OR DIOXOLANES)
         11471 1,3-DIOXOLANE
                 (1(W)3(W)DIOXOLANE)
L9           3 L7 AND 1,3-DIOXOLANE

=> dup rem l9 l8
PROCESSING COMPLETED FOR L9
PROCESSING COMPLETED FOR L8
L10          5 DUP REM L9 L8 (3 DUPLICATES REMOVED)

=> d l10 ibib hitstr abs 1-5

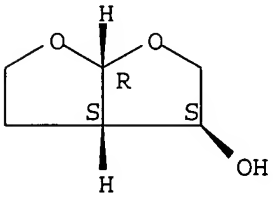
L10  ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2005 ACS on STN  DUPLICATE 1
ACCESSION NUMBER:         2004:333721  CAPLUS
DOCUMENT NUMBER:          140:357319
TITLE:                    Method of preparing (3R,3aS,6aR)-3-
                          hydroxyhexahydrofuro[2,3-b]furan and related compounds
INVENTOR(S):              Ghosh, Arun K.; Leshchenko, Sofiya; Noetzel, Marcus W.
PATENT ASSIGNEE(S):       The Board of Trustees of the University of Illinois,
                          USA
SOURCE:                   PCT Int. Appl., 63 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE       APPLICATION NO.          DATE
     ---------------      ----   --------   --------------------     --------
     WO 2004033462         A2    20040422   WO 2003-US32029          20031008
     WO 2004033462         A3    20040930
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     US 2004127727         A1    20040701   US 2003-681637           20031008
PRIORITY APPLN. INFO.:                      US 2002-417379P      P   20021009
OTHER SOURCE(S):          CASREACT 140:357319; MARPAT 140:357319
IT   681463-05-8P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (claimed compound; stereoselective preparation of
        (3R,3aS,6aR)-3-hydroxyhexahydrofuro[2,3-b]furan and related compds.
        with high enantiomeric selectivity)
RN   681463-05-8  CAPLUS
CN   Furo[2,3-b]furan-3-amine, hexahydro- (9CI)  (CA INDEX NAME)
```



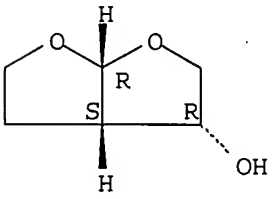
IT **252873-50-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective **preparation** of (3R,3aS,6aR)-3-hydroxyhexahydrofuro[2,3-b]furan and related compds. with high enantiomeric selectivity)
RN 252873-50-0 CAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aS,6aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **156928-09-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(stereoselective **preparation** of (3R,3aS,6aR)-3-hydroxyhexahydrofuro[2,3-b]furan and related compds. with high enantiomeric selectivity)
RN 156928-09-5 CAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



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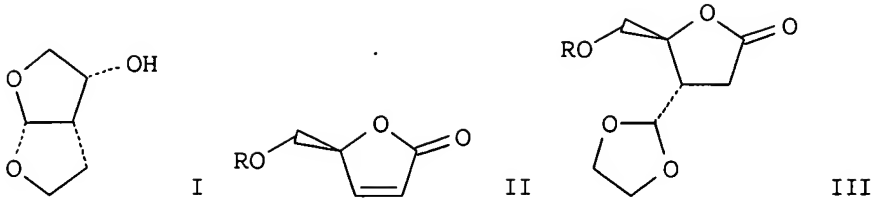
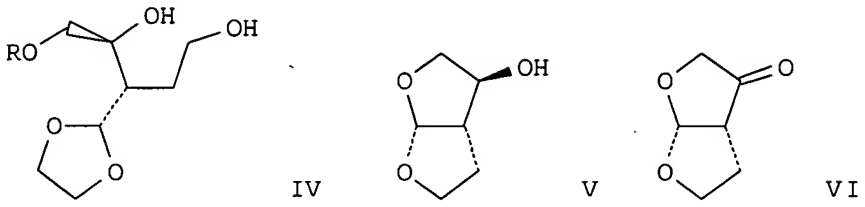
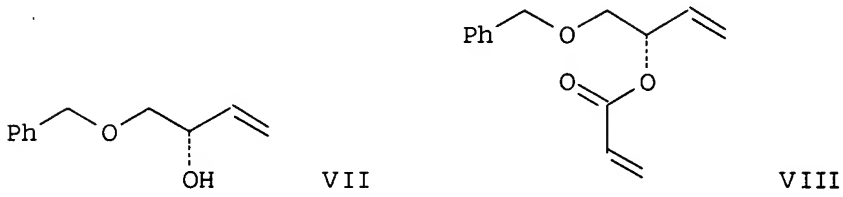






AB A method of **synthesizing** (3R,3aS,6aR)-3-hydroxyhexahydrofuro[2,3-b]furan (I), and related compds., in high yield and high enantiomeric selectivity is disclosed. The above **process** comprises (a) optionally reacting (5S)-hydroxymethyl-5H-furan-2-one (II; R = H) with a compound capable of positioning a protecting group at the hydroxy position to provide a protected furan-2-one II (R = protecting group); (b) subjecting II (R = H) or protected II (R = protecting group) of optional step (a) to a photochem. addition reaction in the presence of **1,3-dioxolane** to provide a 1,3-dioxolan-substituted furan-2-one (III; R = H, protecting group); (c) reducing the compound III to a reduced product (IV; R = H, protecting group), then hydrolyzing the reduced product to provide a product (V) (d) oxidizing the product V to provide a product (VI) and (e) reducing the product VI to provide I. The compound I is an intermediate for several highly potent HIV inhibitors. Also disclosed is a method of manufacturing the compound II which comprising the steps of (a) subjecting (±)-1-(benzyloxy)but-3-en-2-ol to an enzymic acylation using immobilized lipase PS-30 and isopropenyl acetate to provide (S)-1-(benzyloxy)but-3-en-2-ol (VII); (b) reacting the product VII with acryloyl chloride to provide (S)-1-(benzyloxy)but-3-en-2-yl acrylate (VIII); and (c) interacting the product VIII with Grubbs catalyst [Cl2(PCy3)(IMes)Ru:CHC6H5] (metathesis cyclization) to provide II.

L10 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:20676 CAPLUS
DOCUMENT NUMBER: 140:77015
TITLE: **Preparation** of stereoisomers of 3α,3aβ,6aβ-hexahydrofuro[2,3-b]furan-3-ol
INVENTOR(S): Doan, Brian Daniel; Patterson, Daniel Edward; Roberts,

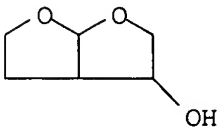
John C.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004002975	A1	20040108	WO 2003-US20094	20030625

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

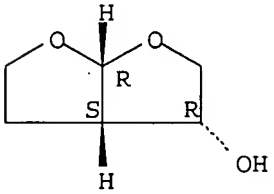
PRIORITY APPLN. INFO.: US 2002-392677P P 20020627

IT **109789-19-7P**, Hexahydrofuro[2,3-b]furan-3-ol
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**preparation** of stereoisomers of 3α,3aβ,6aβ-hexahydrofuro[2,3-b]furan-3-ol via 2,3-dihydrofuran annulation and enzymic resolution)
RN 109789-19-7 CAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro- (9CI) (CA INDEX NAME)



IT **156928-09-5P**, 3R,3AS,6aR-hexahydrofuro[2,3-b]furan-3-ol
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(**preparation** of stereoisomers of 3α,3aβ,6aβ-hexahydrofuro[2,3-b]furan-3-ol via 2,3-dihydrofuran annulation and enzymic resolution)
RN 156928-09-5 CAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



10/681,637R>

AB A **process** for the **preparation** of stereoisomers of 3α,3aβ,6aβ-hexahydrofuro[2,3-b]furan-3-ol is disclosed. For instance, treatment of 2,3-dihydrofuran with Et chlorooxoacetate (MTBE, Et3N) provides Et α-oxo-4,5-dihydrofuran-3-ylacetate as an oil which is reduced to the diol (THF, LAH) and cyclized (THF/H2O, NBS) to give 3a-bromohexahydrofuro[2,3-b]furan-3-ol as a mixture of 2 diastereomers (3:1). This is reduced (THF, Et3N, H2-Pd/C) and acetylated to give acetic acid hexahydrofuro[2,3-b]furan-3-yl ester. Minor isomer acetates are reacted with a lipase (0.1N Na2HPO4, pH 7.0, 35°, PS-800) and the unreacted acetate starting material (organic extract) is deacylated (MeOH, K2CO3) to give 3R,3aS,6aR-hexahydrofuro[2,3-b]furan-3-ol. **Prepn**. of 3a-bromo analogs are also described. Compds. disclosed herein are useful in the **preparation** of compds. that may be inhibitors of HIV aspartyl protease. The current **process** uses inexpensive, nonchiral starting materials and does not rely on heavy metals or **photochem.** compared to prior art methods.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

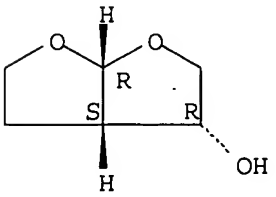
L10 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2004:870349 CAPLUS
DOCUMENT NUMBER: 142:56210
TITLE: Stereoselective Photochemical **1,3-Dioxolane** Addition to 5-Alkoxymethyl-2(5H)-furanone: **Synthesis** of Bis-tetrahydrofuranyl Ligand for HIV Protease Inhibitor UIC-94017 (TMC-114)
AUTHOR(S): Ghosh, Arun K.; Leshchenko, Sofiya; Noetzel, Marcus
CORPORATE SOURCE: Department of Chemistry, University of Illinois at Chicago, Chicago, IL, 60607, USA
SOURCE: Journal of Organic Chemistry (2004), 69(23), 7822-7829 CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:56210

IT **156928-09-5P 252873-50-0P**
RL: BPN (Biosynthetic preparation); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective **preparation** of a nonracemic dioxolanylfuranone by photochem. addition of **1,3-dioxolane** to nonracemic 5-(benzyloxymethyl)-2-furanone and its use in the **preparation** of the HIV protease inhibitor UIC-94017)

RN 156928-09-5 CAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

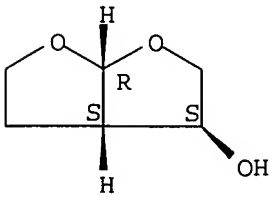


RN 252873-50-0 CAPLUS

10/681,637R>

CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aS,6aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB HIV protease inhibitor UIC-94017 I is prepared using the stereoselective photochem. addition of **1,3-dioxolane** to nonracemic 5-substituted 2-furanones to yield dioxolanylfuranones as the key step. Nonracemic 5-(benzyloxymethyl)-2-furanone II (R = PhCH2) is prepared in 4-7 steps from benzyloxyacetaldehyde using a lipase-mediated resolution to generate the desired absolute stereochem. Addition of vinylmagnesium bromide to benzyloxyacetaldehyde yields 1-(benzyloxy)-3-buten-2-ol which undergoes enantioselective acylation with isopropenyl acetate in the presence of lipase PS-30 to yield (S)-1-(benzyloxy)-3-buten-2-ol in 49% yield and 99% ee and (R)-1-(benzyloxy)-3-buten-2-ol acetate in 49% yield (which can be converted to the desired alc. in 3 steps and 82% yield and 81% ee). Acylation of (S)-1-(benzyloxy)-3-buten-2-ol with acryloyl chloride followed by ring closure with the 2nd generation Grubbs ruthenium metathesis catalyst provides II (R = PhCH2). II [R = Me3CSi(Me)2, Ac, Me3CCO, PhCO, 2-tetrahydropyranyl] are also prepared by a three-step procedure from isopropylidene-D-glycerol. Irradiation of II [R = PhCH2, Me3CSi(Me)2, Ac, Me3CCO, PhCO, 2-tetrahydropyranyl] and **1, 3-dioxolane** in the presence of benzophenone yields dioxolanylfuranones III [R = PhCH2, Me3CSi(Me)2, Ac, Me3CCO, PhCO, 2-tetrahydropyranyl] in 36-93% yields and with 76:24-97:3 selectivity for the trans stereoisomers (in all but one case ≥96:4 stereoselectivity). Reductive cleavage of the benzyl group of III (R = PhCH2), lithium aluminum hydride reduction of the lactone and acid-mediated cyclization yields the alc. epimer of desired hexahydrofurofuranol IV; either oxidation of the alc. to the ketone followed by reduction or Mitsunobu inversion followed by hydrolysis of the p-nitrobenzoate ester yields IV stereoselectively. Ring opening of (S,S)-N-Boc-α-benzyloxiranemethanamine with isobutylamine followed by sulfonylation of the secondary amine with p-nitrobenzenesulfonyl chloride yields intermediate carbamate V. Reduction of the nitro group of V, removal of the Boc group, and coupling with the N-hydroxysuccinimidyl carbonate mixed ester of IV yields I.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2003:242341 CAPLUS
DOCUMENT NUMBER: 138:271663

10/681,637R>

TITLE: **Process** for preparing intermediates for HIV aspartyl protease inhibitors, particularly (3α,3aβ,6aβ)-hexahydrofuro[2,3-b]furan-3-ol and its (3R,3aS,6aR)-enantiomer

INVENTOR(S): Doan, Brian Daniel; Davis, Roman D.; Lovelace, Thomas Claiborne

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA

SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

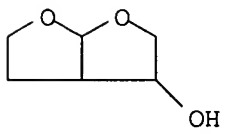
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024974	A2	20030327	WO 2002-US29315	20020916
WO 2003024974	A3	20040729		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1465897	A2	20041013	EP 2002-761678	20020916
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2004204595	A1	20041014	US 2004-490186	20040319
PRIORITY APPLN. INFO.:			US 2001-323692P P	20010920
			WO 2002-US29315 W	20020916

OTHER SOURCE(S): CASREACT 138:271663; MARPAT 138:271663

IT **109789-19-7P**, Hexahydrofuro[2,3-b]furan-3-ol
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(target intermediate; **preparation** of hexahydrofurofuranol racemate and enantiomer as intermediates for HIV aspartyl protease inhibitors)

RN 109789-19-7 CAPLUS

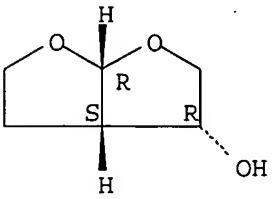
CN Furo[2,3-b]furan-3-ol, hexahydro- (9CI) (CA INDEX NAME)



IT **156928-09-5P**, (3R,3aS,6aR)-Hexahydrofuro[2,3-b]furan-3-ol
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(target intermediate; **preparation** of hexahydrofurofuranol racemate and enantiomer as intermediates for HIV aspartyl protease inhibitors)

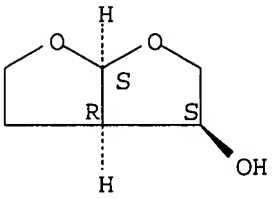
RN 156928-09-5 CAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **162119-33-7P**, (3α,3aβ,6aβ)-Hexahydrofuro[2,3-b]furan-3-ol
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(target intermediate; **preparation** of hexahydrofurofuranol racemate and enantiomer as intermediates for HIV aspartyl protease inhibitors)
RN 162119-33-7 CAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



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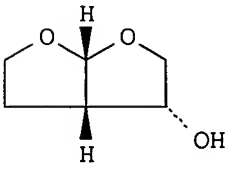

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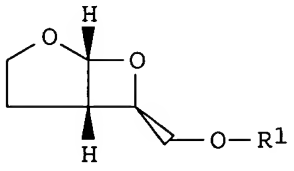

II

AB The invention includes a method for preparing cyclic alcs. I (racemic or enantiomeric). The method involves a reduction, deprotection, and rearrangement, in non-aqueous telescoping conditions, of a bicyclic oxetane derivative II [R1 = C(R2)3, COR3, or Si(R3)3; R2 = (independently) H, alkyl, or aryl; R3 = (independently) alkyl or aryl]. The invention further provides a method of **preparation** of an intermediate useful in the **synthesis** of compds. that function as inhibitors of the aspartyl protease enzyme of human immunodeficiency virus (HIV). For instance, photochem. cycloaddn. of TBDMS-OCH2CHO with furan gave 98% yield of II [R1 = TBDMS, i.e., SiMe2Bu-tert]. The adduct underwent double-bond hydrogenation over water-wet 5% Pt/C in THF in the presence of K2CO3. This was followed (without isolation) by hydrolytic deprotection and

rearrangement in THF solution in the presence of H2O and concentrated HCl, to give (±)-I in 82% yield (both steps). Racemic I was resolved by (1) O-acetylation with Ac2O, Na2CO3, and DMAP; (2) selective hydrolysis of the undesired enantiomer of the acetate using the lipase PS-800 in phosphate buffer at pH 6.8-7.2, giving the (3R,3aS,6aR)-acetate in >98% ee; and (3) hydrolysis using K2CO3 in MeOH at room temperature, giving (3R,3aS,6aR)-I. Other protecting groups for use in R1, namely PhCMe2, tert-Bu, and PhCH2, are exemplified.

L10 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:594851 CAPLUS
DOCUMENT NUMBER: 137:154919
TITLE: **Preparation** of 3-methylenehexahydrofuro[2,3-b]furan via **photochemical** cyclization of 3-halo-2-(2-propynyloxy)tetrahydrofurans.
INVENTOR(S): Davis, Roman; Lovelace, Thomas Clairborne
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002060905	A2	20020808	WO 2001-US46116	20011022
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2002067239	A2	20020829	WO 2001-US51428	20011022
WO 2002067239	A3	20040108		
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EP 1404680	A2	20040407	EP 2001-271082	20011022
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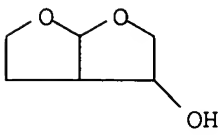
JP 2004519473	T2	20040702	JP 2002-566479	20011022
US 2004026230	A1	20040212	US 2003-399809	20030423
PRIORITY APPLN. INFO.:			US 2000-242822P P	20001024
			WO 2001-US51428 W	20011022

OTHER SOURCE(S): CASREACT 137:154919; MARPAT 137:154919
IT **109789-19-7P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP

(Preparation)
(**preparation** of 3-methylenehexahydrofuro[2,3-b]furan via **photochem.** cyclization of 3-halo-2-(2-propynyloxy)tetrahydrofuran)

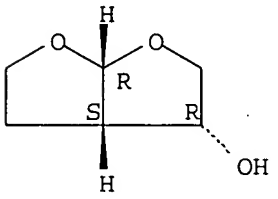
RN 109789-19-7 CAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro- (9CI) (CA INDEX NAME)



IT **156928-09-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(**preparation** of 3-methylenehexahydrofuro[2,3-b]furan via **photochem.** cyclization of 3-halo-2-(2-propynyloxy)tetrahydrofuran)

RN 156928-09-5 CAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



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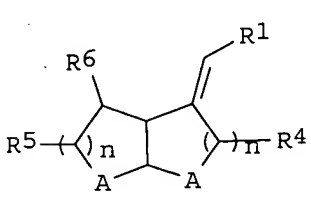

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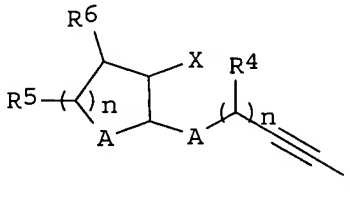

II

AB Title compds. (I; A = CH2, CHR10, CR10R11, O, NH, NR10, S; R10, R11 = H, alkyl, aryl; R1 = H, alkyl, aryl, heterocyclyl, alkylheterocyclyl; R4 = H, alkyl, aryl, alkylheterocyclyl, heterocyclyl; R5 = H, aryl, alkyl, alkylheterocyclyl, OR12, CH2OR12; R12 = alkyl, COR10; R6 = H, aryl, alkyl, alkylheterocyclyl, heterocyclyl, OR12, CH2OR12; n = 1-4), were prepared by exposure of alkynes (II; X = halo; other variables as above) to 200-400 nM light in the presence of NR7R8R9 (R7-R9 = H, aryl, alkyl, alkylheterocyclyl, heterocyclyl). Thus, 3-bromo-2-(2-propynyloxy)tetrahydrofuran in MeCN/Et3N was **irradiated** at 254 nM for 15-20 h to give 3-methylenehexahydrofuro[2,3-b]furan.

10/681,637R>

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=> s l7 and (photochemical or irradiat? or heat)
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            15 PHOTOCHEMICALS
         43577 PHOTOCHEMICAL
                 (PHOTOCHEMICAL OR PHOTOCHEMICALS)
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        146764 PHOTOCHEM
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          3221 IRRADNS
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                 (IRRADIAT? OR IRRADN)
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         53201 HEATS
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10/681,637R>

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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
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NEWS	5	NOV 30	PHAR reloaded with additional data
NEWS	6	DEC 01	LISA now available on STN
NEWS	7	DEC 09	12 databases to be removed from STN on December 31, 2004
NEWS	8	DEC 15	MEDLINE update schedule for December 2004
NEWS	9	DEC 17	ELCOM reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	10	DEC 17	COMPUAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	11	DEC 17	SOLIDSTATE reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	12	DEC 17	CERAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	13	DEC 17	THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB
NEWS	14	DEC 30	EPFULL: New patent full text database to be available on STN
NEWS	15	DEC 30	CAPLUS - PATENT COVERAGE EXPANDED
NEWS	16	JAN 03	No connect-hour charges in EPFULL during January and February 2005
NEWS	17	FEB 25	CA/CAPLUS - Russian Agency for Patents and Trademarks (ROSPATENT) added to list of core patent offices covered
NEWS	18	FEB 10	STN Patent Forums to be held in March 2005
NEWS	19	FEB 16	STN User Update to be held in conjunction with the 229th ACS National Meeting on March 13, 2005
NEWS	20	FEB 28	PATDPAFULL - New display fields provide for legal status data from INPADOC
NEWS	21	FEB 28	BABS - Current-awareness alerts (SDIs) available
NEWS	22	FEB 28	MEDLINE/LMEDLINE reloaded
NEWS	23	MAR 02	GBFULL: New full-text patent database on STN
NEWS	24	MAR 03	REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS	25	MAR 03	MEDLINE file segment of TOXCENTER reloaded

NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN

10/681,637R>

NEWS WWW CAS World Wide Web Site (general information)

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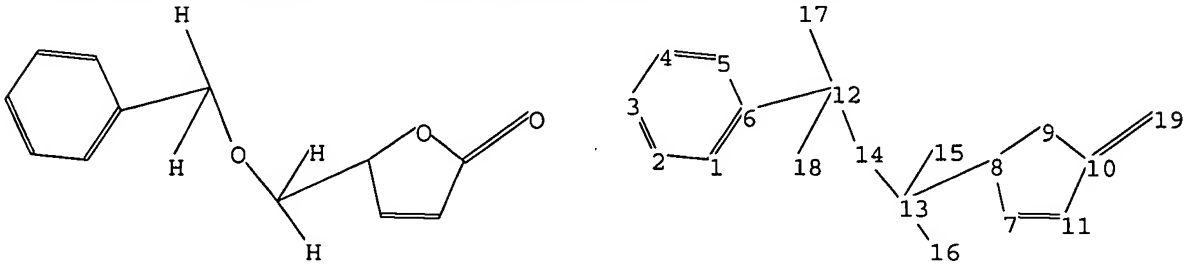

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ring nodes :

10/681,637R>

1 2 3 4 5 6 7 8 9 10 11
chain bonds :
6-12 8-13 10-19 12-14 12-17 12-18 13-14 13-15 13-16
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-11 8-9 9-10 10-11
exact/norm bonds :
7-8 7-11 8-9 9-10 10-11 10-19 12-14 13-14
exact bonds :
6-12 8-13 12-17 12-18 13-15 13-16
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS

L1 STRUCTURE UPLOADED

=> s l1
SAMPLE SEARCH INITIATED 19:41:17 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1556 TO ITERATE

64.3% PROCESSED 1000 ITERATIONS 0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 28754 TO 33486
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 ful
FULL SEARCH INITIATED 19:41:25 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 31211 TO ITERATE

100.0% PROCESSED 31211 ITERATIONS 23 ANSWERS
SEARCH TIME: 00.00.01

L3 23 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 161.33 161.54

FILE 'CAPLUS' ENTERED AT 19:41:36 ON 10 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 10 Mar 2005 VOL 142 ISS 11
FILE LAST UPDATED: 9 Mar 2005 (20050309/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s l3
L4          55 L3

=> s l4 and (process or prepara? or synthes? or make or made)
       2058963 PROCESS
       1372174 PROCESSES
       3061803 PROCESS
                 (PROCESS OR PROCESSES)
       1436714 PREPARA?
       2556211 PREPN
        198603 PREPNS
       2706663 PREPN
                 (PREPN OR PREPNS)
       3469141 PREPARA?
                 (PREPARA? OR PREPN)
       1432482 SYNTHES?
        205351 MAKE
        158511 MAKES
        353636 MAKE
                 (MAKE OR MAKES)
       1137894 MADE
            23 MADES
       1137914 MADE
                 (MADE OR MADES)
L5          53 L4 AND (PROCESS OR PREPARA? OR SYNTHES? OR MAKE OR MADE)

=> s l5 and enzym?
       1044948 ENZYM?
L6           2 L5 AND ENZYM?

=> s l5 and lipase
         43788 LIPASE
          7976 LIPASES
         45012 LIPASE
                 (LIPASE OR LIPASES)
L7           2 L5 AND LIPASE

=> dup rem l7 l6
PROCESSING COMPLETED FOR L7
PROCESSING COMPLETED FOR L6
L8           2 DUP REM L7 L6 (2 DUPLICATES REMOVED)

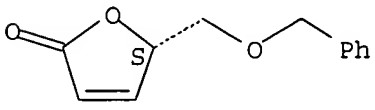
=> d l8 ibib hitstr abs 1-2
```

L8 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2004:333721 CAPLUS
DOCUMENT NUMBER: 140:357319
TITLE: Method of preparing (3R,3aS,6aR)-3-hydroxyhexahydrofuro[2,3-b]furan and related compounds
INVENTOR(S): Ghosh, Arun K.; Leshchenko, Sofiya; Noetzel, Marcus W.
PATENT ASSIGNEE(S): The Board of Trustees of the University of Illinois, USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

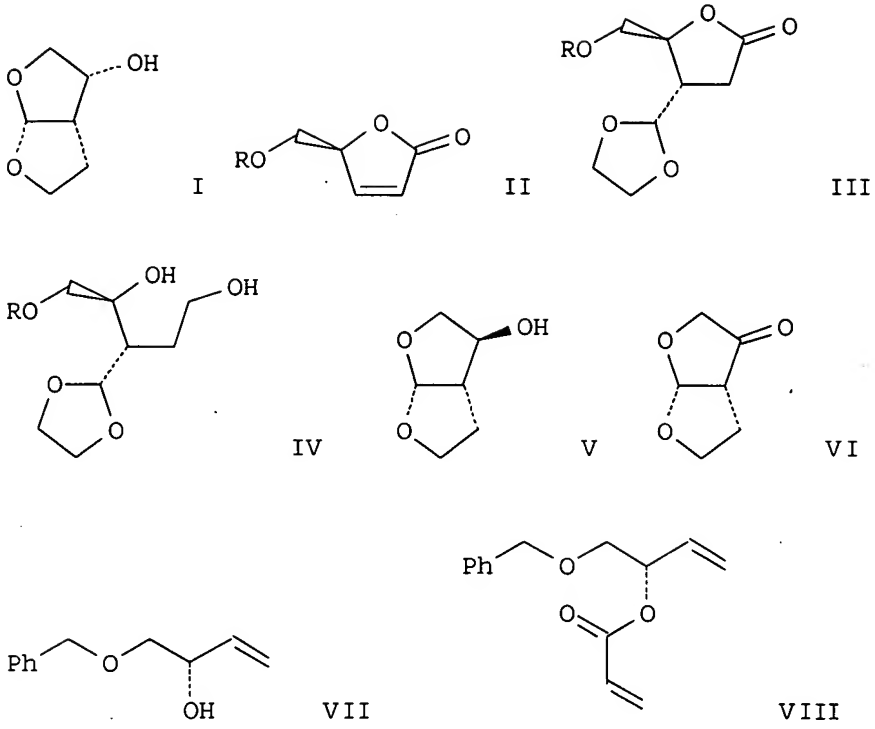
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004033462	A2	20040422	WO 2003-US32029	20031008
WO 2004033462	A3	20040930		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004127727	A1	20040701	US 2003-681637	20031008
PRIORITY APPLN. INFO.:			US 2002-417379P P	20021009

OTHER SOURCE(S): CASREACT 140:357319; MARPAT 140:357319
IT **72605-53-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective **preparation** of (3R,3aS,6aR)-3-hydroxyhexahydrofuro[2,3-b]furan and related compds. with high enantiomeric selectivity)
RN 72605-53-9 CAPLUS
CN 2(5H)-Furanone, 5-[(phenylmethoxy)methyl]-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



GI



AB A method of **synthesizing** (3R,3aS,6aR)-3-hydroxyhexahydrofuro[2,3-b]furan (I), and related compds., in high yield and high enantiomeric selectivity is disclosed. The above **process** comprises (a) optionally reacting (5S)-hydroxymethyl-5H-furan-2-one (II; R = H) with a compound capable of positioning a protecting group at the hydroxy position to provide a protected furan-2-one II (R = protecting group); (b) subjecting II (R = H) or protected II (R = protecting group) of optional step (a) to a photochem. addition reaction in the presence of 1,3-dioxolane to provide a 1,3-dioxolan-substituted furan-2-one (III; R = H, protecting group); (c) reducing the compound III to a reduced product (IV; R = H, protecting group), then hydrolyzing the reduced product to provide a product (V) (d) oxidizing the product V to provide a product (VI). and (e) reducing the product VI to provide I. The compound I is an intermediate for several highly potent HIV inhibitors. Also disclosed is a method of manufacturing the compound II which comprising the steps of (a) subjecting (±)-1-(benzyloxy)but-3-en-2-ol to an enzymic acylation using immobilized **lipase** PS-30 and isopropenyl acetate to provide (S)-1-(benzyloxy)but-3-en-2-ol (VII); (b) reacting the product VII with acryloyl chloride to provide (S)-1-(benzyloxy)but-3-en-2-yl acrylate (VIII); and (c) interacting the product VIII with Grubbs catalyst [Cl2(PCy3)(IMes)Ru:CHC6H5] (metathesis cyclization) to provide II.

L8 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2004:870349 CAPLUS

DOCUMENT NUMBER: 142:56210

TITLE: Stereoselective Photochemical 1,3-Dioxolane Addition to 5-Alkoxymethyl-2(5H)-furanone: **Synthesis** of Bis-tetrahydrofuranyl Ligand for HIV Protease Inhibitor UIC-94017 (TMC-114)

AUTHOR(S): Ghosh, Arun K.; Leshchenko, Sofiya; Noetzel, Marcus

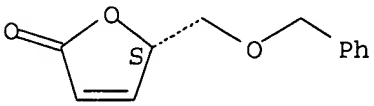
10/681,637R>

CORPORATE SOURCE: Department of Chemistry, University of Illinois at Chicago, Chicago, IL, 60607, USA
SOURCE: Journal of Organic Chemistry (2004), 69(23), 7822-7829
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:56210

IT **72605-53-9P**
RL: BPN (Biosynthetic preparation); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(**preparation** of nonracemic 5-(benzyloxymethyl)-2-furanone using a **lipase**-mediated resolution and its use in the **preparation** of the HIV protease inhibitor UIC-94017 using a stereoselective photochem. addition as the key step)

RN 72605-53-9 CAPLUS
CN 2(5H)-Furanone, 5-[(phenylmethoxy)methyl]-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB HIV protease inhibitor UIC-94017 I is prepared using the stereoselective photochem. addition of 1,3-dioxolane to nonracemic 5-substituted 2-furanones to yield dioxolanylfuranones as the key step. Nonracemic 5-(benzyloxymethyl)-2-furanone II (R = PhCH2) is prepared in 4-7 steps from benzyloxyacetaldehyde using a **lipase**-mediated resolution to generate the desired absolute stereochem. Addition of vinylmagnesium bromide to benzyloxyacetaldehyde yields 1-(benzyloxy)-3-buten-2-ol which undergoes enantioselective acylation with isopropenyl acetate in the presence of **lipase** PS-30 to yield (S)-1-(benzyloxy)-3-buten-2-ol in 49% yield and 99% ee and (R)-1-(benzyloxy)-3-buten-2-ol acetate in 49% yield (which can be converted to the desired alc. in 3 steps and 82% yield and 81% ee). Acylation of (S)-1-(benzyloxy)-3-buten-2-ol with acryloyl chloride followed by ring closure with the 2nd generation Grubbs ruthenium metathesis catalyst provides II (R = PhCH2). II [R = Me3CSi(Me)2, Ac, Me3CCO, PhCO, 2-tetrahydropyranyl] are also prepared by a three-step procedure from isopropylidene-D-glycerol. Irradiation of II [R = PhCH2, Me3CSi(Me)2, Ac, Me3CCO, PhCO, 2-tetrahydropyranyl] and 1,3-dioxolane in the presence of benzophenone yields dioxolanylfuranones III [R = PhCH2, Me3CSi(Me)2, Ac, Me3CCO, PhCO, 2-tetrahydropyranyl] in 36-93% yields and with 76:24-97:3 selectivity for the trans stereoisomers (in all but one case ≥96:4 stereoselectivity). Reductive cleavage of the benzyl group of III (R = PhCH2), lithium aluminum hydride reduction of the lactone and acid-mediated cyclization yields the alc. epimer of desired hexahydrofurofuranol IV; either oxidation of the alc. to the ketone followed

by reduction or Mitsunobu inversion followed by hydrolysis of the p-nitrobenzoate ester yields IV stereoselectively. Ring opening of (S,S)-N-Boc-α-benzyloxiranemethanamine with isobutylamine followed by sulfonylation of the secondary amine with p-nitrobenzenesulfonyl chloride yields intermediate carbamate V. Reduction of the nitro group of V, removal of the Boc group, and coupling with the N-hydroxysuccinimidyl carbonate mixed ester of IV yields I.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	25.36	186.90

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.46	-1.46

STN INTERNATIONAL LOGOFF AT 19:44:27 ON 10 MAR 2005